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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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ENZO BIOCHEM, INC.
527 MADISON AVENUE (9TH FLOOR)
NEW YORK, NY 10022

EXAMINER	
LU, FRANK WEI MIN	
ART UNIT	**PAPER NUMBER**
1634	
MAIL DATE	**DELIVERY MODE**
10/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/898,750	WETMUR ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *117-178* is/are pending in the application.

4a) Of the above claim(s) *126,133,138,139,142,143 and 149-178* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *117-125,127-132,134-137,140,141 and 144-148* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission of RCE, the amendment, and oath/declaration filed on August 9, 2007 have been entered. The claims pending in this application are claims 117-178 wherein claims 126, 133, 138, 142, 143, and 149-178 have been withdrawn due to restriction requirement and species election. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of the response filed on August 9, 2007.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. New Matter

Claims 117-125, 127-132, 134-137, 140, 141, and 144-148 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The limitation "wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide" is added to the newly amended independent claim 117. In view of page 6, lines 19-32, page 8, lines 27-33, and page 19, lines 17-26 of specification suggested by applicant, the examiner cannot locate where in the specification supports such claim recitation.

MPEP 2163.06 notes "IF NEW MATTER IS ADDED TO THE CLAIMS, THE EXAMINER SHOULD REJECT THE CLAIMS UNDER 35 U.S.C. 112, FIRST PARAGRAPH - WRITTEN DESCRIPTION REQUIREMENT. *IN RE RASMUSSEN*, 650 F.2D 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application." MPEP 2163.06 further notes "WHEN AN AMENDMENT IS FILED IN REPLY TO AN OBJECTION OR REJECTION BASED ON 35 U.S.C. 112, FIRST PARAGRAPH, A STUDY OF THE ENTIRE APPLICATION IS OFTEN NECESSARY TO DETERMINE WHETHER OR NOT "NEW MATTER" IS INVOLVED. *APPLICANT SHOULD THEREFORE SPECIFICALLY POINT OUT THE SUPPORT FOR ANY AMENDMENTS MADE TO THE DISCLOSURE*" (emphasis added).

Response to Arguments

In page 12, third and fourth paragraphs of applicant's remarks, applicant argues that "[A]pplicants respectfully direct the Examiner's attention to the paragraph entitled 'Claim Amendments' on page 13 of the Response dated November 17, 2006. Support for the above-mentioned amendments may be found at page 6, lines 19-32; page 8, lines 27-33; and page 19, lines 17-26 of the originally filed specification. Withdrawal of the rejection is respectfully requested".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, in view of page 6, lines 19-32 and page 8, lines 27-33 of the specification suggested by applicant, the examiner cannot locate the support for the limitation

"wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide" recited in claim 117. Second, although page 19, lines 17-26 of the specification describes that "[O]ne of the significant uses of our invention is for the site specific addition or deletion of nucleotides in a recipient polydeoxynucleotide sequence. This process occurs when the new strand is introduced to the recipient duplex and displaces the original strand. The cellular machinery involved in generalized recombination and gene conversion will act to transfer sequence information from the displacer strand to the recipient polydeoxynucleotide", since the limitation "wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide" recited in claim 117 can be read as "wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the **single or double** stranded recipient polynucleotide" and claim 117 does not limit a recipient polynucleotide as a double stranded nucleic acid, the limitation "wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide" recited in claim 117 is much broader than "wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the double stranded recipient polynucleotide" described by the specification. Therefore, the limitation "wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide" recited in claim 117 is a new matter.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 117-119, 121, 125, 134-136, 144, and 145 are rejected under 35 U.S.C. 102(e) as being anticipated by Lin et al., (US Patent No. 5,214,136, filed on February 20, 1990).

Regarding claim 117, Lin *et al.,* teach a nucleic acid displacer composition comprising an isolated oligo-or polynucleotide displacer (ie., 5'-P-CCC-TCT-TTT-TTT-CCP in Table 4) which complexes with to a recipient polynucleotide (ie., a single stranded RNA), said oligo- or polynucleotide displacer comprising two or more sequences: a) at least one first sequence which complexes with said recipient polynucleotide (ie., CCC-TCT in 5'-P-CCC-TCT-TTT-TTT-CCP in Table 4); b) at least one second sequence (ie., TT-TTT in 5'-P-CCC-TCT-TTT-TTT-CCP in Table 4), said second sequence being complementary to at least a portion of said recipient polynucleotide, comprising one or more modified nucleotides (ie., CP in 3' of 5'-P-CCC-TCT-TTT-TTT-CCP) that increase stability; and comprising one or more nucleotides that form a mismatch (ie., T in 6 position in 5'-P-CCC-TCT-TTT-TTT-CCP in Table 4) with the recipient polynucleotide as recited in the claim (see columns 8-10 and Table 4). Since the nucleic acid displacer taught by Lin *et al.,* has an ability to changes at least one nucleotide or a nucleotide sequence in the recipient polynucleotide taught by Lin *et al.,* when the displacer is introduced into the recipient polynucleotide, the recipient polynucleotide recited in the claim is not a part of

a nucleic acid displacer composition, and the phrase "wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide" is not a structural limitation of the claim but is a functional limitation of the claim, Lin *et al.,* teach said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide as recited in the claim.

Regarding claims 118, 119, and 121, Lin *et al.,* teach that said second sequence is adjacent to said first sequence as recited in claim 118 wherein said second sequence is separated from said first sequence by from 1 to 5 intervening moieties (ie., T in 6 position in 5'-P-CCC-TCT-TTT-TTT-CCP in Table 4) as recited in claim 119 and said intervening moieties are nucleotides as recited in claim 121 (see columns 8-10 and Table 4).

Regarding claim 125, Lin *et al.,* teach that least one of said nucleotides complementary to one strand of the recipient polynucleotide is modified to increase the stability of the displacer-recipient complex, wherein the modification is in the second sequence (ie., CP in 3' of 5'-P-CCC-TCT-TTT-TTT-CCP) (see columns 8-10 and Table 4).

Regarding claims 134-136, since Lin *et al.,* teach that 5'-P-CCC-TCT-TTT-TTT-CCP is resistant to snake venom phosphodiesterase digestion, it is known that snake venom phosphodiesterase is an exonuclease (see page 1 of attachment for snake venom phosphodiesterase), and claim 134 does not require that at least one moiety attached to a terminus of the oligo or polynucleotide is different from the one modified nucleotide recited in claim 117, Lin *et al.,* disclose at least one moiety attached to a terminus of the oligo or polynucleotide, said moiety conferring exonuclease resistance to the terminus to which it is

attached as recited in claim 134 wherein said moiety is attached to a terminal nucleotide (ie., anthraquinone of P in 3' of 5'-P-CCC-TCT-TTT-TTT-CCP) as recited in claim 135 and said moiety is indirectly attached to a terminal nucleotide as recited in claim 136 (ie., by P in 3' of 5'-P-CCC-TCT-TTT-TTT-CCP) (see columns 8-10 and Table 4).

Regarding claims 144 and 145, Lin *et al.*, teach further comprising a modification (ie., a fluorescent label) which permits detection of the displacer-recipient complex as recited in claim 144 wherein said modification comprises a member selected from the group consisting of non-radioactive labels, radioactive labels, fluorescent labels, chemiluminescent labels, enzymes and targets for detection as recited in claim 145 (see column 5, lines 51-64).

Therefore, Lin *et al.*, teach all limitations recited in claims 117-119, 121, 125, 134-136, 144, and 145.

Response to Arguments

In page 13, first paragraph bridging to page 14, first paragraph of applicant's remarks, applicant argues that "the instant claims are drawn to a nucleic acid displacer composition comprising an isolated single-stranded oligo-or polynucleotide displacer wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide. This differs from Lin *et al.* in that the claimed oligo-or polynucleotide displacer changes at least one nucleotide or nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide. While the Office Action asserts that the 'displacer' of Lin *et al.* 'changes at least one nucleotide or nucleotide sequence in the receipt polynucleotide', Applicants can not find support for this in Lin *et al.* Office Action at 5. It appears that the Examiner is referring to

Example 5, 'Specificity of Hybridization' for support that Lin *et al.* teach that the displacer changes at least one nucleotide or a nucleotide sequence in the recipient polynucleotide when the displacer is introduced into the recipient polynucleotide. Col. 9, line 9 through Col. 10, line 15. However, a closer reading of this section gives no indication that the displacer changes a nucleotide in the recipient ploynucleotide. Here, the oligomers containing the anthraquinone-conjugated polynucleotides were evaluated with regard to hybridization specificity as compared to controls (oligomers which do not contain the anthraquinone). The anthraquinone-conjugated polynucleotide oligomer (which the Examiner has labeled a 'displacer' and contains a mismatch) are complexed to a single-stranded RNA molecule. The authors then measured the changes in melting temperatures caused by the single base-pair mismatch in the *oligomer,* as opposed to the single-stranded RNA molecule (recipient polynucleotide). There is no indication in Example 5, or anywhere else in the reference, that Lin *et al.* teaches or contemplates a displacer that changes a nucleotide in the recipient ploynucleotide. Each and every limitation of independent claim 117, and the claims depending from claim 117, is not taught or suggested by the cited reference".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. Although Lin *et al.,* do not directly teach changes at least one nucleotide or a nucleotide sequence in the recipient polynucleotide, since the nucleic acid displacer taught by Lin *et al.,* has an ability to changes at least one nucleotide or a nucleotide sequence in the recipient polynucleotide taught by Lin *et al.,* when the displacer is introduced into the recipient polynucleotide, the recipient polynucleotide recited in claim 117 is not a part of a nucleic acid displacer composition, and the phrase "wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is

introduced into the recipient polynucleotide" recited in claim 117 is not a structural limitation of the claim but is a functional limitation of the claim, Lin *et al.*, do teach said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide as recited in the claim.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 146 and 147 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lin *et al.*, as applied to claims 117-119, 121, 125, 134-136, 144, and 145 above, and further in view of Dattagupta *et al.*, (US Patent No. 4,737,454, published on April 12, 1988).

The teachings of Lin *et al.*, have been summarized previously, *supra*.

Lin *et al.*, do not disclose that said modification in claim 144 is selected from the group consisting of biotin moieties, phosphorothioate linkages and antigens as recited in claim 146 and a modification which allows capture of the displacer-recipient complex by affinity chromatography as recited in claim 147.

Regarding claims 146 and 147, Since Dattagupta *et al.*, teach that a nucleic acid probe can be labeled with hapten or biotin, an enzyme such as a β-galactosidase or horse radish peroxidase, a fluorescent radical, a phycobiliprotein, a luminescent radical, or a radioisotope (see abstract) and it is known that biotin binds to avidin, Dattagupta *et al.*, disclose that said modification (ie., biotin) in claim 144 is selected from the group consisting of biotin moieties, phosphorothioate linkages and antigens as recited in claim 146 and a modification which allows capture of the displacer-recipient complex by affinity chromatography (ie., the affinity chromatography comprising avidin) as recited in claim 147.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have made the displacer recited in claims 146 and 147 wherein said modification is biotin moieties and the modification (ie., biotin) which allows capture of the displacer-recipient complex by affinity chromatography (ie., the affinity chromatography comprising avidin) in view of the prior art of Lin *et al.*, and Dattagupta *et al.*.

One having ordinary skill in the art would have been motivated to do so because the simple replacement of one kind of label (ie., the fluorescent label taught by Lin *et al.*, see column 5, lines 51-64) from another kind of label (ie., the biotin label taught by Dattagupta *et al.*,) during the process of labeling the displacer recited in claims 146 and 147, in the absence of convincing evidence to the contrary, would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made since the label taught by Lin *et al.*, and the label taught by Dattagupta *et al.*, are used for the same purpose (ie., labeling a nucleic acid probe).

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

Response to Arguments

In page 14, third paragraph bridging to page 17, third paragraph of applicant's remarks, applicant argues that: (1) "[A]s discussed above, Lin *et al.* does not disclose the instantly claimed displacer that changes a nucleotide in the recipient polynucleotide. Applicants submit that the references cited in the Office Action do not individually or in combination suggest to a person of ordinary skill in the art the invention of the Applicants' dependent claims 146 and 147, which incorporate all of the elements of independent claim 117. The Office Action fails to establish why or how it would have been obvious to one of ordinary skill in the art at the time of the

invention to combine Lin *et al.* with Dattagupta *et al.* to produce an oligo- or polydeoxynucleotide displacer meeting all the limitations of claims 146 and 147"; (2) "[E]ven if, *arguendo,* it were proper to combine the references, it has not been established in the Office Action that the combination would have yielded a composition that meets each and every limitation of the claims. The Dattagupta *et al.* reference does not cure the deficiencies of Lin *et al.* Dattagupta *et al.* discloses a labeled nucleic acid probe for detection in hybridization assays and for the determination of specific polynucleotide sequences. See Abstract. The probe is labeled by means of photochemistry and employs a photoreactive nucleic acid binding ligand. Col 1, lines 39-54. Nowhere does Dattagupta *et al.* teach the displacer molecule of Applicants' presently claimed invention. The Lin *et al.* modified oligonucleotide sequences are distinct. Absent an explicit teaching or a suggestion in Lin *et al.,* it would not have been obvious to a person of ordinary skill in the art to modify the oligonucleotide sequences described therein. Thus, a person of ordinary skill in the art would not have found it obvious to combine the teachings of the cited references because neither Lin *et al.* nor Dattagupta *et al.* teaches each and every limitation of the claims. The improper combination of the references fail to suggest to a person of ordinary skill in the art the use of the oligonucleotide sequences of Lin *et al.* to produce the isolated single-stranded oligo-or polynucleotide displacer wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide, as required by claim 117"; and (3) "the Examiner is incorrectly describing the use of labels by Lin *et al.* Lin *et al.* does not disclose DNA probes. The anthraquinone is used as an agent to increase stability, not as a label. In fact, the detection of anthraquinone is not described at all. There is no evidence that the derivative use

of anthraquinone has fluorescent properties that would enable it to be used as a label for detecting DNA-DNA hybridization".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, although Lin *et al.*, do not directly teach changes at least one nucleotide or a nucleotide sequence in the recipient polynucleotide, since the nucleic acid displacer taught by Lin *et al.*, has an ability to changes at least one nucleotide or a nucleotide sequence in the recipient polynucleotide taught by Lin *et al.*, when the displacer is introduced into the recipient polynucleotide, the recipient polynucleotide recited in claim 117 is not a part of a nucleic acid displacer composition, and the phrase "wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide" recited in claim 117 is not a structural limitation of the claim but is a functional limitation of the claim, Lin *et al.*, do teach said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide as recited in the claim. Second, applicant's statement "[T]he Office Action fails to establish why or how it would have been obvious to one of ordinary skill in the art at the time of the invention to combine Lin *et al.* with Dattagupta *et al.* to produce an oligo- or polydeoxynucleotide displacer meeting all the limitations of claims 146 and 147" is incorrect since there is a motivation to combine the references from Lin *et al.*, and Dattagupta *et al.*, (see above office action). Third, applicant's statement "[L]in *et al.* does not disclose DNA probes" is incorrect because the oligomers taught by Lin *et al.*, is DNA probes (see Column 10, Table 4). Fourth, the examiner does not indicate that anthraquinone is used as a label as argued by applicant.

8. Claim 148 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lin *et al.*, as applied to claims 117-119, 121, 125, and 134-136 above.

The teachings of Lin *et al.*, have been summarized previously, *supra*.

Lin *et al.*, do not disclose an artificially constructed polynucleotide hybrid comprising a naturally occurring recipient polynucleotide duplex hybridized to the nucleic acid displacer composition of claim 118 as recited in claim 148.

However, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have made an artificially constructed polynucleotide hybrid comprising a naturally occurring recipient polynucleotide duplex hybridized to the nucleic acid displacer composition of claim 118 as recited in claim 148 by hybridizing the nucleic acid displacer composition of claim 118 to a naturally occurring RNA. One having ordinary skill in the art would have been motivated to do so because Lin *et al.*, tested the oligonucleotide coupled to anthraquinone *in vitro* and *in vivo* (see column 7, lines 49-51) and hybridized the oligonucleotide coupled to anthraquinone to a single stranded RNA (see column 9) and one having ordinary skill in the art would select a hybridized target nucleic acid such as a naturally occurring RNA based on his or her experimental requirements. One having ordinary skill in the art at the time the invention was made would have a reasonable expectation of success to make an artificially constructed polynucleotide hybrid comprising a naturally occurring recipient polynucleotide duplex hybridized to the nucleic acid displacer composition of claim 118 as recited in claim 148 by hybridizing the nucleic acid displacer composition of claim 118 to a naturally occurring RNA.

Response to Arguments

In page 17, third paragraph bridging to page 18, first paragraph of applicant's remarks, applicant argues that "[A]s discussed above, Lin *et al.* does not describe the instantly claimed oligo-or polynucleotide displacer meeting all the limitations of dependent claim 148, which incorporates all of the elements of independent claim 117. Specifically, Lin et *al.* does not teach a displacer that changes a nucleotide in the recipient polynucleotide. Thus, there would be no motivation to alter the Lin *et al.* displacer to form an artificially constructed polynucleotide comprising a naturally occurring recipient polynucleotide duplex hybrid to the nucleic acid displacer composition. There would be no expectation of success because the altered composition would not result in Applicants presently claimed invention".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, although Lin *et al.,* do not directly teach changes at least one nucleotide or a nucleotide sequence in the recipient polynucleotide, since the nucleic acid displacer taught by Lin *et al.,* has an ability to changes at least one nucleotide or a nucleotide sequence in the recipient polynucleotide taught by Lin *et al.,* when the displacer is introduced into the recipient polynucleotide, the recipient polynucleotide recited in claim 117 is not a part of a nucleic acid displacer composition, and the phrase "wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide" recited in claim 117 is not a structural limitation of the claim but is a functional limitation of the claim, Lin *et al.,* do teach said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide as recited in the claim. Second, there is a

motivation to alter the Lin *et al.* displacer to form an artificially constructed polynucleotide comprising a naturally occurring recipient polynucleotide duplex hybrid to the nucleic acid displacer composition (see above office action). Third, applicant has no evidence to show that it would be no reasonable expectation of success to make an artificially constructed polynucleotide hybrid comprising a naturally occurring recipient polynucleotide duplex hybridized to the nucleic acid displacer composition of claim 118 as recited in claim 148 by hybridizing the nucleic acid displacer composition of claim 118 to a naturally occurring RNA.

Conclusion

9. This is a RCE of applicant's earlier Application No. 09/898,750. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however,

event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. No claim is allowed.

11. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

October 9, 2007

FRANK LU
PRIMARY EXAMINER